

from the syringe through a 14-gauge cannula to form ribbons of the paste. Some of the mixture was formed by hand into a desired shape. The material was then allowed to anneal for about 20 min, without being disturbed. After annealing, some of the ribbon was placed in tap water to soak (B74-W).

The products prepared as described above have the following characteristics:

When initially mixed it is a paste which can be ejected through a standard syringe. Subsequent batches of this mixture have been injected into rats subcutaneously, intramuscularly and also into the intermedullary canal of rat femurs.

The mixture anneals to a hard, polycrystalline, ceramic-like material.

X-ray diffraction (XRD) analysis of the material which was not placed in water shows it to contain the following mineral phases:

- 1) Calcite — CaCO_3 ;
- 2) Hydroxyapatite — $\text{Ca}_5(\text{PO}_4)_3(\text{OH})$;
- 3) Dibasic Sodium Phosphate, dihydrate — $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$;
- 4) Sodium Bicarbonate — NaHCO_3 .

X-ray diffraction (XRD) analysis of the material which was placed in water shows it to contain the following mineral phases:

- 1) Calcite — CaCO_3 ;
- 2) Hydroxyapatite — $\text{Ca}_5(\text{PO}_4)_3(\text{OH})$.

Example 3

SB w/BioFibre TM

An alkaline solution was prepared of 5.4 g of sodium hydroxide pellets in 19.0 ml of distilled water. A powder was prepared of 9.8 g of orthophosphoric acid crystals, 8.0 g of calcium carbonate, 1.5 g of calcium hydroxide, and 5.0 g of BioFibre¹⁹⁸ (microcrystalline hydroxyapatite fibers). The powders were mixed and ground together until thoroughly dispersed. The 19 ml of sodium hydroxide solution was poured into the mixed powders and mixed for about 1 to 2 min until a paste was formed. The mixture was formed into the desired shape, and was then allowed to anneal for about 20 min, without being disturbed.

The products prepared as described above have the following characteristics:

The mixture anneals to a hard, polycrystalline, ceramic-like material, which feels stiffer than the material produced in Example 2

Example 4

SB w/Collagen

A slurry was prepared containing 0.6 g of collagen for each 13.6 g of distilled water, and heated 35° C. for 1-2 days. An alkaline solution was prepared of 5.4 g of sodium hydroxide pellets in 5.4 g of distilled water. A powder was prepared of 9.8 g of orthophosphoric acid crystals, 8.0 g of calcium carbonate, 1.5 g of calcium hydroxide, and 5.0 g of hydroxyapatite crystal nuclei. The powders were mixed and ground together until thoroughly dispersed, and then 14.2 g of the collagen slurry was poured into the powders, followed by the 10.8 g of sodium hydroxide solution. The solutions were

mixed into the powders for about 1 to 2 min until a paste was formed. The mixture was formed into the desired shape, and was then allowed to anneal for about 20 min, without being disturbed.

The products prepared as described above have the following characteristics:

The mixture anneals to a hard, polycrystalline, ceramic-like material, which is tougher and more viscoelastic than the material produced in Example 2 (B74 recipe) and Example 3 (BioFibreTM recipe).

It is evident from the above results, that the subject methods and compositions provide a unique alternative to other methods for producing hydroxyapatite. In accordance with this method, compositions can be produced which can be allowed to harden in situ, so as to be placed in position and fill any spaces. The mixture will then harden to a shaped product which may then be modified, if desired, to fit a particular site, so that it may be machined, worked, or otherwise formed.

All publications and patent applications mentioned in this specification are indicative of the level of skill of those skilled in the art to which this invention pertains. All publications and patent applications are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be obvious that certain changes and modifications may be practiced within the scope of the appended claims.

What is claimed is:

1. A method for making calcium phosphate minerals comprising:

combining phosphoric acid substantially free of uncombined water, a calcium source, neutralizing anions including at least one of carbonate, phosphate and hydroxide in an amount sufficient to substantially neutralise said phosphoric acid and water in an amount to provide a kneadable mixture at a physiologically acceptable temperature; agitating the mixture to produce a substantially uniform mixture; and allowing the mixture to set and become annealed to a hard workable structure.

2. A method according to claim 1, wherein (calcium phosphate) crystals are combined in said combining step.

3. A method according to claim 1, wherein said phosphoric acid is orthophosphoric acid crystals.

4. A method according to claim 3, wherein the orthophosphoric acid and calcium source are premixed prior to combining with water.

5. A method according to claim 1, wherein said calcium source is present at least in part as calcium carbonate.

6. A method according to claim 1, wherein a protein is combined in said combining step.

7. A method for making hydroxyapatite comprising: combining orthophosphoric acid crystals, calcium carbonate, at least one of alkali metal or calcium hydroxide in an amount to provide a substantially neutral mixture, at a physiologically acceptable temperature, and water in an amount to provide a kneadable product;